TABLE 1

Ethanol and Water Content of Azithromycin Ethanolate

Batch	Ethanol Content (gas chromatography) % w/w (weight/weight)	Water Content (Karl-Fischer) % w/w
A	2.2	3.24
B	2.3	2.46
C	2.2	2.71
D	2.3	2.77
E	2.2	3.28
F	1.52	2.70
G	1.7	3.40

In accordance with the present invention, the new ethanolate of azithromycin may be prepared as pharmaceutical compositions that are particularly useful for the treatment of infections caused by susceptible microorganisms. Such compositions comprise the new ethanolate of azithromycin with pharmaceutically acceptable carriers and/or excipients.

For example, these compositions may be prepared as medicines to be administered orally, parenterally, rectally, transdermally, bucally, or nasally. Suitable forms for oral administration include tablets, compressed or coated pills, dragees, sachets of powder for reconstitution, hard or gelatin capsules, sub-lingual tablets, syrups and suspensions. Suitable forms for parenteral administration include an aqueous or non-aqueous solution or emulsion, while for rectal administration suitable forms include suppositories with hydrophilic or hydrophobic vehicles. For topical application the invention provides ointments or aerosol formulations known in the art; for transdermal delivery there are provided suitable delivery systems as known in the art. For nasal delivery there are provided suitable aerosol delivery systems known in the art.

Experimental Details

Hygroscopicity profiles were obtained by maintaining samples in controlled humidity chambers for a period of two weeks, followed by Karl Fisher analysis of water content.

Gas chromatograms were obtained using a Hewlett-Packard 5890 gas chromatograph.

Powder x-ray diffraction patterns were obtained by methods known in the art using a Philips X-Ray powder diffractometer, Goniometer model 1050/70 at a scanning speed of 2° per minute, with a Cu radiation of λ=1.5418 Å.

This invention will be better understood from the Example that follows. However, the examples illustrate, but do not limit, the invention. Those skilled in the art will readily appreciate that the specific methods and results discussed are merely illustrative of the invention as described more fully in the claims that follow thereafter.

EXAMPLE

Preparation of Azithromycin Ethanolate.

Ten g of azithromycin crude was introduced into a 0.25 liter three-necked flat flanged jacketed vessel equipped with a mechanical stirrer, a condenser and thermometer and containing 30 ml of absolute ethanol at 20° C. Three ml of water at 20° C. were added and the solution was heated at a constant temperature gradient so as to reach 55° C. after 4 hours. Between 35° C. and 55° C., additional water having a total volume of 11 ml was slowly added at regular time intervals. When 55° C. was reached, the resulting suspension was maintained at this temperature for 2 hours, during which an additional 49 mL of water was added. The suspension was then cooled from 55° C. to 20° C. over 2 hours. The precipitate was filtered. After drying, 9 g of azithromycin ethanolate were obtained.

Although certain presently preferred embodiments of the invention have been described herein, it will be apparent to those skilled in the art to which the invention pertains that variations and modifications of the described embodiments may be made without departing from the spirit and scope of the invention. Accordingly, it is intended that the invention be limited only to the extent required by the appended claims and the applicable rules of law.

We claim:

1. An ethanolate of azithromycin having an ethanol content of about 1.5% to about 3%.

2. The ethanolate of claim 1, having a water content of about 2% to about 4%.

3. The ethanolate of claim 2, wherein the water content is between about 2.5% and about 3.5%.

4. The ethanolate of claim 1, wherein the ethanol content is about 1.5% to about 2.5%.

5. The ethanolate of claim 4, wherein the water content is about 2% to about 4%.

6. The ethanolate of claim 5, wherein the water content is between about 1.5% and about 2.5%.

7. An ethanolate of azithromycin that is characterized by a powder x-ray diffraction pattern substantially as depicted in FIG. 2.

8. A method of making an ethanolate of azithromycin, comprising the steps of:

forming an azithromycin solution by dissolving azithromycin in ethanol;

adding water to the azithromycin solution such that crystallization of the azithromycin begins and a suspension is formed; and,

isolating the crystals of azithromycin.

9. The method of claim 8, further comprising maintaining the suspension at a temperature from about 30° C. to about 80° C. for a period of time, following the step of adding water to the azithromycin solution.

10. The method of claim 8, further comprising adding additional water to the suspension, and maintaining the suspension at a temperature from about 30° C. to about 80° C. for about 1 hour to about 18 hours, following the step of adding water to the azithromycin solution.

11. The method of claim 8, further comprising cooling the suspension to about 20° C., prior to the step of isolating the crystals of azithromycin.

12. The method of claim 8, wherein the ethanolate of azithromycin has an ethanol content of about 1.5% to about 3%.

13. The method of claim 8, wherein the ethanolate of azithromycin has a water content of about 2% to about 4%.

14. The method of claim 8, wherein the ethanolate is characterized by a powder x-ray diffraction pattern substantially as depicted in FIG. 2.

15. A pharmaceutical composition comprising a therapeutically effective amount of the ethanolate of the claim 1 and a pharmaceutically acceptable carrier.

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